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EXAMINER	
SALMON, KATHERINE D	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,657	WADA ET AL.	
	Examiner	Art Unit	
	KATHERINE SALMON	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9-27,29,35-44,51,53,55,59-65,67-75,83,86,92-95 and 97-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9-27,29,35-44,51,53,55,59-65,67-75,83,86,92-95 and 97-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/26/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed 3/26/2008. Currently Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 are pending. Claims 2, 5-7, 28, 30, 33-34, 45-50, 52, 54, 76-77, 80-82, 85, 87, 90have been cancelled.

2. The following rejections for Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 are newly applied. It is noted that the claims are being rejected as anticipated by Kawabata et al. This interpretation of the art reference of Kawabata et al is newly applied as the reference teach polyanions other than heparin which were not previously discussed.

3. This action is NONFINAL

Interview

4. It is noted that the applicant has acknowledges the telephone interview on February 29, 2008 (p. 19 2nd paragraph).

Withdrawn Rejections/Objections

5. The applicant asserts that the office action of 10/02/2007 stated that the rejection of Claims 37-40 and 95-97 made under 35 USC 112/2nd paragraph in section 6 in view of the cancellation of the claims (p. 19 last paragraph). However, it is acknowledged that the rejection of the claims was moot based upon the amendments to the claims and not the cancellation. It is noted that Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 are pending

Claim Rejections - 35 USC § 102

6. The following rejections are necessitated by amendment. It is noted that Kawabata et al. is used in the following region, however, the teachings of heparin in Kawabata et al. is not used as the teaching of the polyanion in step ii, therefore, the arguments towards the use of heparin in Kawabata et al. presented in the reply are moot.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 are rejected under 35 U.S.C. 102(b) as being anticipated by Kawabata et al. (EP 1376126A1 3/04/2002)

With regard to Claim 1, Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a

molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

With regard to Claims 3-4, Kawabata et al. teaches the polyanion is polyvinyl (p. 12 paragraphs 57-59).

With regard to Claims 9 and 22, Kawabata et al. teaches a nucleic acid chain affinity substance is labeled with a marker (Figure 2).

With regard to Claim 10, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (analyte) (Figure2). Claims 16-18 defines nucleic acids as having a negative charge. Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

With regard to Claims 11, 12, and 13, Kawabata et al. teaches the binding of "protein" and "peptide chain"; "antigen" and "antibody"; "sugar chain" and "lectin"; "enzyme" and "inhibitor"; and "receptor" and "ligand" (p. 6 paragraph 20).

With regard to Claim 14, Kawabata et al. teaches the charged carrier molecule is a nucleic acid chain (anionic) (p. 3-4 paragraph 6).

With regard to Claim 15, the charged carrier molecule is a nucleic acid chain (negative charge) and the charged polymer is a polyvinyl (negative charge).
With regard to Claims 16-17, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6).

With regard to Claims 18, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6). Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 6 paragraph 15).

With regard to Claims 19-21, Kawabata et al. teaches a method of labeling the nucleic acid with a linker, such as, Sulfo-SMPB (sulfosuccinimidyl) (succinimide group) (p. 7 paragraph 22 and p. 9 paragraph 32).

With regard to Claims 23-24, Kawabata et al teaches a nucleic acid chain attached to an affinity substance and labeled with a marker (Figure 2). The conjugate is the nucleic acid chain attached to the affinity substance. With regard to Claim 25, Kawabata et al. teaches the nucleic acid chain is labeled (Figure 2).

Claim 26 is drawn to an affinity molecule in the conjugate, which is labeled by a detectable marker. The claim is not limited to a label, which is directly connected to the affinity or directly connected with a linker to an affinity. Therefore, since in the conjugate the nucleic acid is directly attached to the affinity and the nucleic acid is

labeled the affinity would be labeled. Kawabata et al. teaches a method using an Alexa488-labeled anti-AFP antibody Fab' fragment (p. 24 p. 152).

With regard to Claim 27, Kawabata et al. teaches the use of fluorescent dyes and radioactive tracers (p. 8 paragraph 26).

With regard to Claim 29, Kawabata et al. teaches the separation media can be comprised of polyethylene glycol, polyacrylamide, polyethylene oxide, or polyvinylpyrrolidone (p. 12, paragraph 59).

With regard to Claim 35, Kawabata et al. teaches the diameter of the capillary channel (cross sectional microscale dimension) of between 1 to 200 microns (p. 12 paragraph 58).

With regard to Claim 36, Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 74). Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract).

Claim 37 has every limitation of Claim 10, but also includes the limitation that two or more conjugates are used wherein each affinity molecule is capable of binding the analyte at a different site. Kawabata et al. teaches at least two affinity molecules (in a complex) which bind to the target (analyte) at different sites (Figure 4). With regard to Claim 95, Kawabata et al. teach at least two affinity molecules which bind to the target (analyte) at different sites (Figure 4).

Claim 38 has every limitation of Claim 10, but also the limitation that the affinity molecule and the affinity molecule in the conjugate have a property capable of binding to the analyte at a different site on the analyte form every other affinity molecule. Kawabata et al. teaches a method in which the nucleic acid (charged carrier molecule), affinity molecules, and analytes are in a solution together (Figure 2). Kawabata et al. teaches at least two affinity molecules (in a complex) which bind to the target (analyte) at different sites (Figure 4).

With regard to Claims 39-41 and 97-99, Kawabata teaches a method in which an analyte, affinity, and a charge polymer form a complex which is labeled (first complex) (Figure 6). The claim does not limit how the analyte is labeled so therefore a conjugate comprising the analyte, affinity, and a labeled charged polymer would encompass the claims. Kawabata et al. teaches 2 or more of these complexes can be made (Figure 6). Kawabata et al. teaches separating the sample (Figure 6). Kawabata et al. teaches 2 or more affinity molecules can be used (Figure 6). Kawabata et al. teaches measuring and determining the amount of analyte in the sample (Abstract). Kawabata et al. teaches at least two affinity molecules which bind to the target (analyte) at different sites (Figure 4).

With regard to Claim 42, it is unclear in the claim which combination is actually needed in the first complex. With regard to the first complex, Kawabata et al. teaches contacting the sample with a complex of analyte, affinity, and detectable marker (figure 2). Since the analyte is labeled in this complex because of the attachment of the labeled charged molecule it is unclear what the difference it between the first and

second complex. Kawabata et al, teaches 2 or more types of targets can be labeled (forming 2 or more complexes) and separated (Figure 6). Further Kawabata et al. teaches that two ore more affinity molecules may be used in the separation (Figure 6). With regard to Claim 100, Kawabata et al. teaches at least two affinity molecules which bind to the target (analyte) at different sites (Figure 4).

With regard to Claim 43, Kawabata et al. teaches targets comprising serum, plasma, urine, feces, and environmental samples (p. 11 paragraph 49).

With regard to Claim 44, Kawabata et al. teaches a target comprising AFP, FSH, TSH, LH, HIV, CA10-19, CA125, PSA, or T4 (p. 5 paragraph 56).

With regard to Claim 51, Kawabata et al. teaches contacting a sample, with an affinity attached to a nucleic acid chain, which is labeled (Figure 2). Kawabata et al. teaches separating the complex using capillary electrophoresis (p. 12 paragraph 58). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). For the first capillary, the sample is concentrated because only the sample that goes through the entire first capillary is introduced into the capillary for separation; therefore, the first capillary is a concentration channel. Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54). Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (analyte)

(Figure2). Kawabata et al. teaches the addition of the charged substance improves separation ability (p. 2-3 paragraph 9).

With regard to Claim 53, Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54). Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). Therefore the complex goes through a concentration channel (first capillary) and then to the separation capillary in a solution stopping at a reservoir between the two capillaries (microchannel fluidically).

With regard to Claim 55, Kawabata et al. teaches that retention time (electrophoretic mobility) was different between the labeled conjugate and the antibody alone (noise constituents) (p. 27 paragraph 170). Kawabata et al. teaches that separation ability is improved with the use of a charged substance (p. 2-3 paragraph 9).

With regard to Claims 59-61, Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6).

With regard to Claim 62, Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 6 paragraph 15).

With regard to Claims 63-65, Kawabata et al. teaches a method of labeling the nucleic acid with a linker, such as, Sulfo-SMPB (sulfosuccinimidyl) (succinimide group) (p. 7 paragraph 22 and p. 9 paragraph 32).

With regard to Claim 67, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) attached to an affinity substance attached to a target (analyte) (Figure2).

With regard to Claims 68-69, Kawabata et al. teaches the binding of "protein" and "peptide chain"(protein: protein interaction); "antigen" and "antibody"; "sugar chain" and "lectin"; "enzyme" and "inhibitor"; and "receptor" and "ligand" (p. 6 paragraph 20).

With regard to Claim 70, Kawabata et al. teaches the affinity molecule can be FAB, $F(ab')_2$ (p. 6 paragraph 21).

With regard to Claim 71, Kawabata et al teaches a nucleic acid chain attached to an affinity substance and labeled with a marker (Figure 2). The conjugate is the nucleic acid chain attached to the affinity substance.

Claim 74 is drawn to an affinity molecule in the conjugate, which is labeled by a detectable marker. The claim is not limited to a label, which is directly connected to the affinity or directly connected with a linker to an affinity. Therefore, since in the conjugate the nucleic acid is directly attached to the affinity and the nucleic acid is labeled the affinity would be labeled. Kawabata et al. teaches a method using an Alexa488-labeled anti-AFP antibody Fab' fragment (p. 24 paragraph 152).

With regard to Claims 72-73, Kawabata et al. teaches an affinity attached to a nucleic acid chain, which is labeled (Figure 2).

With regard to Claim 75, Kawabata et al. teaches the use of fluorescent dyes and radioactive tracers (p. 8 paragraph 26).

With regard to Claim 83, Kawabata et al. teaches a nucleic acid chain (charge carrier molecule) and heparin (charged polymer) (Figure 2, p. 23 paragraphs 144-145). Both the nucleic acid chain and heparin are negatively charged.

With regard to Claims 86, Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). Kawabata et al. teaches the capillary is filled with a filler such as, polyethylene glycol, polyethylene oxide, polyvinylpyrroliodone, and polyacrylamide (p. 12 paragraph 59).

With regard to Claim 92, Kawabata et al. teaches the capillary used is 100 micron or less (p. 11-12 paragraph 54).

With regard to Claim 93, Kawabata et al. teaches a method of capillary chip electrophoresis comprising adding a buffer and sample to a sample reservoir, applying voltage and migrating the sample through a capillary wherein the sample which goes completely through the first capillary is introduced into a capillary for separation (p. 12 paragraph 56 and Figure 7). Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 2 paragraph 8). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13, paragraph 74). Kawabata et al. teaches a method for

measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

With regard to Claim 94, Kawabata et al. teaches at least two affinity molecules which bind to the target (analyte) at different sites (Figure 4).
However, Kawabata et al. does not teach filling a separation channel with a separation media and a charged polymer before separation.

With regard to Claim 96, Kawabata et al. teaches at least two affinity molecules which bind to the target (analyte) at different sites (Figure 4).

Response to Arguments

It is noted that Kawabata et al. was previously used in the 35 USC 103(a) rejection in the previously filed office action (10/02/2007). In that office action the examiner rejected the claims based upon the teaching of Kawabata et al. and Krylov et al. with regard to heparin. However, that rejection has been removed because Kawabata et al. and Krylov et al. do not teach heparin added to the separation media. As such the arguments presented in regard to heparin on p. 22-23 of the reply are moot.

The reply asserts that the claimed methods involve an affinity molecule that contacts an analyte of interests prior to separation or concentration step plus a polyanion added to the separation media I the separation channel (p. 23 1st paragraph). The reply asserts that Kawabata et al. does not cite a separation channel filled with a separation media and a polyanion added to the media (p. 23 3rd paragraph).

This argument has been fully reviewed but has not been found persuasive.

Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Therefore Kawabata et al. teaches a capillary tube filled with both a separation media and a polyanion.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 4, 8, 79, 84, and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) as applied to Claims 1,

3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 in the rejection above and in view of Stalcup et al. (Analytical Chemistry 1994 Vol. 66 p. 3054).

Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Kawabata et al. does not teach that the polyanion added to the separation media is heparin sulfate.

With regard to Claims 4, 8, 79, 84, and 91, Stalcup et al. teaches using 2% heparin in the phosphate buffer in capillary zone electrophoresis (abstract).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include 2% concentration of charged polymers of heparin in a buffer

as taught by Stalcup et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include 2% concentration or charged polymers in a buffer as taught by Stalcup et al., because Stalcup et al. teaches the highly anionic character of heparin enhances its aqueous solubility while offering the potential for considerable electrophoretic mobility and therefore has utility as a chiral mobile phase additive in capillary zone electrophoresis (p. 3054 1st column 2nd paragraph).

Response to Arguments

The reply traverses that rejection. The reply asserts that Kawabata et al. does not teach all the limitations of the independent claims (p. 26 last paragraph). The reply asserts that Stalcup et al. teaches adding 2% heparin in a phosphate run buffer and as such the capillary contains no separation or concentration media (p. 27 1st paragraph).

These arguments have been fully reviewed but have not been persuasive.

Kawabata et al. provides all the limitations of the independent claims. Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Therefore Kawabata et al. teaches a capillary tube filled with both a separation media and a polyanion. However, Kawabata et al. does not teach polyanion added to the separation media is

heparin sulfate. Stalcup et al. teaches using 2% heparin in the phosphate buffer in capillary zone electrophoresis (abstract).

Though Stalcup et al. does not teach adding heparin to a separation media, Stalcup et al. does teach adding the heparin to the solution which is used to run the sample. It would be prima facie obvious to modify Kawabata et al's teaching of a separation media and a polyanion to include the heparin as the polyanion. The ordinary artisan would be motivated to put heparin in the separation media of Kawabata et al. because Stalcup et al. teaches the highly anionic character of heparin enhances its aqueous solubility while offering the potential for considerable electrophoretic mobility and therefore has utility as a chiral mobile phase additive in capillary zone electrophoresis (p. 3054 1st column 2nd paragraph).

11. Claims 31-32 and 88-89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) as applied to Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 in the rejection above in further view of Stathakis et al. (Journal of Chromatography A 1998 Vol. 817 p. 227).

Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity

molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

However, Kawabata et al. does not teach a charged polymer with a concentration of about 0.01 to 5% or 0.001 to 1%..

With regard to Claims 30 and 87, Stathakis et al. teaches a coating on the capillary electrophoresis silica fuse glass, which contains dextran sulfate or polyvinyl suphonic acid (PVS) (abstract and p. 230 2nd column Section 3.3).

With regard to Claims 31-32 and 88-89, Stathakis et al. teaches a method using 0.001-0.1% dextran or 0.001-1% PVS (p. 230 last paragraph).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include charged polymers in a particular concentration in the separation media as taught by Stathakis et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include charged polymers in separation media as taught by Stathakis et al., because Stathakis

et al. teaches polymers incorporated in the separation buffer can improve migration time reproducibility (p. 229 2nd column 1st sentence).

Response to Arguments

The reply traverses the rejection. The reply asserts the art presented in the rejection do not teach a separation channel in a microfluidic device filled with separation media and a charged polymer (p. 25 last paragraph). This argument has been thoroughly considered but has not been found persuasive. As discussed above in the rejection of Kawabata et al. teaches all the limitations of the independent claim, as such it teaches a separation channel filled with a separation media and a charged polymer. Kawabata et al., however, does not teach the limitation of the dependent claim that a charged polymer with a concentration of about 0.01 to 5% or 0.001 to 1%. However, Stathakis et al. teaches a method using 0.001-0.1% dextran or 0.001-1% PVS (p. 230 last paragraph).

12. Claim 66 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) as applied to 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 in the rejection above in further view of Fukui et al. (Nucleic acid Research, 1996 Vol. 24 p. 3962).

Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an

affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Kawabata et al. teaches the charged carrier is a nucleic acid chain (nucleotide chain, DNA) (p. 3-4 paragraph 6). Kawabata et al. teaches the nucleic acid chain used may be prepared by chemical synthesis (synthetic) (p. 6 paragraph 15).

Therefore Kawabata et al. teach synthetic sequences, however, do not teach a synthetic sequence consisting of a nucleotide that contains a methylene group in the place of the oxygen in the ribose ring.

Fukui et al. teaches linking ACMA to DNA (abstract). With regard to Claim 66, Fukui et al. teaches the ACMA is connecter through a tri-pentamethylene linker (Abstract). Therefore, Fukui et al. teaches a synthetic sequence consisting of a linker, which has a methylene group.

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method comprising synthetic sequences with one or more linker groups of Kawabata et al. to include the specific methylene linker as taught by Fukui et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include methylene linker as taught by Fukui et al., because Fukui et al. teaches a pentamethylene linker which stabilizes the connection between ACMA and the DNA (Abstract) can be used to attach labeling constants to the DNA.

Response to Arguments

The reply traverses the rejection. The reply asserts the art presented in the rejection do not teach a separation channel in a microfluidic device filled with separation media and a charged polymer (p. 27 last paragraph). . This argument has been thoroughly considered but has not been found persuasive. As discussed above in the rejection of Kawabata et al. teaches all the limitations of the independent claim, as such it teaches a separation channel filled with a separation media and a charged polymer. However, with regard to the dependent claims Kawabata et al. does not teach a synthetic sequence consisting of a nucleotide that contains a methylene group in the place of the oxygen in the ribose ring. Fukui et al. teaches the ACMA is connecter through a tri-pentamethylene linker (Abstract). Therefore, Fukui et al. teaches a synthetic sequence consisting of a linker, which has a methylene group.

13. Claims 57-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) as applied to Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 in the rejection above in further view of Kaniansky et al. (Analytical chemistry 2000 Vol. 72 p. 3596).

Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a method for measuring (detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Therefore, Kawabata et al. teach concentrating the analyte, however, do not teach the concentration using isotachophoresis (ITP).

With regard to Claims 57-58, Kaniansky et al. teaches a method of using a capillary electrophoresis chip with a two separation channel coupling (Abstract).

Kaniansky et al. teaches using ITP as a concentration pretreatment of the analyte (Abstract).

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include the ITP concentration method as taught by Kaniansky et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include the ITP concentration method as taught by Kaniansky et al. because Kaniansky et al. teaches using an ITP concentration pretreatment quantified test analytes by 1-2% RSD (Abstract). Kaniansky et al. teaches a well-defined ITP concentration of the analyte can be integrated into the separation method of a capillary channel chip (Abstract).

Response to Arguments

The reply traverses the rejection. The reply asserts the art presented in the rejection do not teach a separation channel in a microfluidic device filled with separation media and a charged polymer (p. 28 last paragraph). . This argument has been thoroughly considered but has not been found persuasive. As discussed above in the rejection of Kawabata et al. teaches all the limitations of the independent claim, as such it teaches a separation channel filled with a separation media and a charged polymer. However, Kawabata et al. does not teach all the limitations of the dependent claims. Kawabata et al. teach concentrating the analyte, however, do not teach the concentration using isotachophoresis (ITP). Kaniansky et al. teaches a method of using

a capillary electrophoresis chip with a two separation channel coupling (Abstract). Kaniansky et al. teaches using ITP as a concentration pretreatment of the analyte (Abstract).

14. Claims 56-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kawabata et al. (EP 1376126A1 3/04/2002) as applied to Claims 1, 3-4, 9-27, 29, 35-44, 51, 53, 55, 59-65, 67-75, 83, 86, 92-99 in the rejection above in further view of Wolfe et al. (Electrophoresis March 23, 2002 Vol. 23 p. 727).

Kawabata et al. teaches a method of measuring a target (detecting an analyte) (Abstract). Kawabata et al. teaches a target substance (analyte) is reacted with an affinity molecule forming a complex (p. 1 paragraph 0008). Kawabata et al. teaches the separation of the complex from nucleic acid chain-binding affinity substances not involved in the formation of the complex (separation of the complex and unbound affinity molecule) (p. 13 paragraph 73). Kawabata et al. teaches adding to a capillary a buffer for migration (e.g. a separation media) and a polymer having a molecular sieve effect (p. 12 paragraphs 56-59). Kawabata et al. teaches that one type of polymer can be polyvinyl (e.g. a polyanion) (paragraph 59). Kawabata et al. teaches separating the complex using capillary electrophoresis with a channel diameter preferably 1 to 200 microns (p. 12 paragraph 58). Kawabata et al. teaches a method for measuring

(detecting) a target separated by complexing with a nucleic acid chain-binding affinity substance (abstract).

Therefore, Kawabata et al. teach concentrating the analyte, however, do not teach that the concentration based on adsorption of the charged carrier.

With regard to Claims 56-57, Wolfe et al. teaches the incorporation of a silica-based solid phase extraction (SPE) system into a microchip platform (the same platform described by Kawabata et al) (Abstract). Wolfe et al. teaches the extraction procedure utilizes the adsorption of DNA onto bare silica (abstract). Wolfe et al. teaches that DNA is removed from the sample load solution and is retained in the washing step (p. 732 1st column last paragraph). Therefore DNA is adsorbed while "noise constituents" are washed away.

Therefore it would be prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the capillary electrophoresis method of Kawabata et al. to include the SPE concentration method as taught by Wolfe et al. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include the SPE concentration method as taught by Wolfe et al. because Wolfe et al. teaches a method of concentrating DNA (so therefore the charged carrier attached to the affinity molecule and the analyte) from noise constituents in the sample by adhering the DNA onto a silica wall (Abstract). The ordinary artisan would be motivated to use the SPE concentration method because Wolfe et al. teaches the extraction of nanogram quantities of DNA in less than 25

minutes (abstract). The ordinary artisan would be motivated to concentrate the charge carrier, affinity, and analyte from noise constituents in a fast and efficient manner.

Response to Arguments

The reply traverses the rejection. The reply asserts the art presented in the rejection do not teach a separation channel in a microfluidic device filled with separation media and a charged polymer (p. 29 last full paragraph). The reply asserts that Wolf et al. does not teach a concentration channel but rather a procedure wherein DNA is adsorbed onto bare silica (p. 29 last full paragraph).

This argument has been thoroughly considered but has not been found persuasive.

As discussed above in the rejection of Kawabata et al. teaches all the limitations of the independent claim, as such it teaches a separation channel filled with a separation media and a charged polymer. Further, thought Wolf et al. does not teach a concentration channel, Kawabata et al. does teach such a limitation. The ordinary artisan would have been motivated to modify the capillary electrophoresis method of Kawabata et al. to include the SPE concentration method as taught by Wolfe et al. because Wolfe et al. teaches a method of concentrating DNA (so therefore the charged carrier attached to the affinity molecule and the analyte) from noise constituents in the sample by adhering the DNA onto a silica wall (Abstract). The ordinary artisan would be motivated to use the SPE concentration method because Wolfe et al. teaches the extraction of nanogram quantities of DNA in less than 25 minutes (abstract). The

ordinary artisan would be motivated to concentrate the charge carrier, affinity, and analyte from noise constituents in a fast and efficient manner.

Conclusion

15. No Claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Katherine Salmon/
Examiner, Art Unit 1634

/Ram R. Shukla/
Supervisory Patent Examiner, Art Unit 1634